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Letter to the Editor

Female gender and atrial fibrillation:

An association with worse prognosis and outcomes

regarding article “Gender-related differences and risk of cardiovascular morbidity and all-cause mortality in patients hospitalized with incident atrial fibrillation without concomitant diseases: A nationwide cohort study of 9519 patients” by Andersson L et al, International Journal of Cardiology; doi: 10.1016/j.ijcard.2014.09.092

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To the Editor:

Females with atrial fibrillation (AF) are at increased risk for ischemic stroke but have been under-represented in AF cohorts. Without anticoagulation, women are at higher risk than men for AF-related thromboembolic events (TE) but results are not consistent (1, 2). Interestingly, vascular complication rates after AF ablation had been recently shown to be also higher in females (3). Female sex has been included in the CHA₂DS₂-VASc score for assessing thromboembolic risk, which doubles in women between the ages of 55 and 65, the menopausal period, when estradiol levels decrease by about 60% (4). Following the menopause, a decline in endogenous estrogen receptors contributes to an up-regulated production of inflammatory cytokines, with further links to the hypercoagulable state (5).

Thus, it was with great interest that we read the article by Andersson and co-workers (6) on the gender-related differences in risk of cardiovascular morbidity and all-cause mortality in patients with lone and idiopathic AF. Using by far the largest nationwide set of patients with incident AF and no other co-morbidity at the time of diagnosis, the authors demonstrated a two-fold risk of thromboembolic events and three-fold increased risk of heart failure in patients with AF irrespective of age and gender, as compared to controls. Furthermore, the authors found that women were at higher risk of stroke and transient ischemic attack than men. The annual rate of thromboembolic events in men and women between 55 and 64 years was 1.0-1.1% and in controls, 0.4% and 0.3%, respectively. This is in accordance with other observational and registry studies that demonstrated low annual rates of thromboembolism (stroke and systemic embolism, TE) in selected populations after AF catheter ablation, reaching event rates that are comparable to patients without AF (7).

The authors should be congratulated for their interesting findings on this topical and timely performed study that are in accordance with our research (8). Assessing gender-specific differences in thromboembolic risk post-ablation and the predictive risk factors for thromboembolism separately in females and males, we found that the incidence of thromboembolic events after AF catheter ablation is low in both genders. In contrast to the current study (6), there were no differences between thromboembolic events in males and females (1.2% versus 2.0%, $p=0.128$). In females, low ejection fraction (EF) and higher CHA₂DS₂-VASc score were independent predictors for thromboembolic risk, while renal dysfunction and all three stroke risk stratification scores, i.e. CHADS₂, CHA₂DS₂-VASc, R₂CHADS₂, were associated with thromboembolic events risk in males. Because men constitute the large part of ablation cohorts, it was perhaps unsurprising to find an association between renal dysfunction and thromboembolic risk scores, as previously demonstrated (8).

Heart failure has been associated with higher stroke rates in AF (9). Whilst impaired left ventricular ejection fraction is more commonly been used as an equivalent for the heart failure, AF patients with heart failure and *normal* (preserved) EF also have greater thromboembolic risk compared with only AF patients (10). Our finding that impaired EF is significant predictor for TE in females supports previous studies; however, the novel aspect is the importance of EF for risk assessment in women after catheter ablation. Demonstrating higher risk for of thromboembolic complications and development of heart failure in females with lone/idiopathic AF, the current study by Andersson et al (6) supports our observations and emphasizes the necessity of more careful gender-specific stroke risk assessment.

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